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PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant	:	Panaccio, et al.	Group Art Unit Unknown
Int'l. Appl. No.:		PCT/AU00/00437	
Int'l Filing Date	:	May 11, 2000	
For	:	LAWSONIA DERIVED GENE AND RELATED FLGE POLYPEPTIDES, PEPTIDES AND PROTEINS AND THEIR USES	
Examiner	:	Unknown	

PRELIMINARY AMENDMENT

Assistant Commissioner for Patents
Washington, D.C. 20231

Dear Sir:

Preliminary to Examination on the merits, please amend the above-captioned patent application as follows:

IN THE SPECIFICATION

On page 1, after the Title of the Invention (on line 1) and before the "Field of the Invention" (on line 4) please insert the following: --This is the U.S. National phase under 35 U.S.C. §371 of International application PCT/AU00/00437, filed May 11, 2000, and claim priority to U.S.Provisional Application 60/133973, filed May 13, 1999, both of which are herein incorporated by reference.--.

IN THE CLAIMS

Please cancel Claims 5, 9, 12, 15, and 16.

Please replace the remaining claims as follows:

1. **(Amended)** An isolated or recombinant immunogenic polypeptide comprising a *Lawsonia spp.* FigE Polypeptide, a variant, or a truncated variant thereof, wherein said variant

or truncated variant mimics or cross-reacts with a B-cell or T-cell epitope of *Lawsonia spp.* FigE Polypeptide.

2. **(Amended)** The isolated or recombinant immunogenic polypeptide of claim 1 wherein said polypeptide elicits the production of antibodies against *Lawsonia* spp. when administered to an avian or porcine animal.

3. **(Amended)** The isolated or recombinant immunogenic polypeptide of claim 1 which confers a protective immune response against *Lawsonia spp.* when administered to an avian or porcine animal.

4. **(Amended)** The isolated or recombinant immunogenic polypeptide of claim 1 wherein the *Lawsonia spp. is L. intracellularis.*

6. **(Amended)** An isolated or recombinant immunogenic polypeptide comprising:

(i) a peptide, oligopeptide or polypeptide comprising an amino acid sequence which has at least about 60% sequence identity to the amino acid sequence set forth in SEQ ID NO: 1; or

(ii) a homologue or derivative of (i) which mimics a B-cell or T-cell epitope of a Lawsonia spp. *FigE polypeptide.*

7. **(Amended)** The isolated or recombinant immunogenic polypeptide of claim 6 wherein said polypeptide elicits the production of antibodies against *Lawsonia* spp. in a porcine or avian animal.

8. **(Amended)** The isolated or recombinant immunogenic polypeptide of claim 7 wherein said polypeptide confers a protective immune response against *Lawsonia spp. in* a porcine or avian animal.

10. **(Amended)** The isolated or recombinant immunogenic polypeptide of claim 8, wherein said protective immune response is induced in a porcine animal.

11. **(Amended)** The isolated or recombinant immunogenic polypeptide of claim 6 wherein the *Lawsonia spp.* is *L. intracellularis.*

13. **(Amended)** The isolated or recombinant immunogenic polypeptide of claim 6 comprising the amino acid sequence set forth in SEQ ID NO: 1 or the amino acid sequence encoded by the FigE-encoding nucleotide sequence of pALK11 (ATCC 207156).

14. **(Amended)** The isolated or recombinant immunogenic polypeptide of claim 13 consisting essentially of the amino acid sequence of SEQ ID NO: 1 or the amino acid sequence encoded by the FigE-encoding nucleotide sequence of pALK11 (ATCC 207156).

17. **(Amended)** A vaccine composition for the prophylaxis or treatment of infection of an animal by *Lawsonia* spp., said vaccine composition comprising an immunogenic component comprising an isolated or recombinant polypeptide having at least about 60% sequence identity to the amino acid sequence set forth in SEQ ID NO: 1 or an immunogenic homologue, or derivative thereof which is immunologically cross-reactive with *Lawsonia intracellularis;* and one or more carriers, diluents or adjuvants suitable for veterinary or pharmaceutical use.

19. **(Amended)** The vaccine composition according to claim 16 wherein the isolated or recombinant polypeptide comprises the amino acid sequence set forth in SEQ ID NO: 1 or the amino acid sequence encoded by the FigE-encoding nucleotide sequence of pALK11 (ATCC 207156).

20. **(Amended)** The vaccine composition of claim 19, wherein the isolated or recombinant polypeptide consists essentially of the amino acid sequence of SEQ ID NO: 1.

21. **(Amended)** A combination vaccine composition for the prophylaxis or treatment of the infection of an animal by *Lawsonia* spp., said vaccine composition comprising:

(i) a first immunogenic component comprising an isolated or recombinant polypeptide having at least about 60% sequence identity to the amino acid sequence set forth in SEQ ID NO: 1 or an immunogenic homologue or derivative thereof which is immunologically cross-reactive with Lawsonia intracellularis;

(ii) a second immunogenic component comprising an antigenic L. intracellularis *peptide, polypeptide or protein; and*

(iii) one or more carriers, diluents or adjuvants suitable for veterinary or pharmaceutical use.

22. **(Amended)** A vaccine vector comprising a polynucleotide that encodes the immunogenic polypeptide of SEQ ID NO: 1, a homologue or a variant thereof operably linked to a promoter.

23. **(Amended)** The vaccine vector of claim 22 wherein the polynucleotide comprises SEQ ID NO: 2 a homologue, or derivative thereof which has at least about 60% sequence identity thereto.

25. **(Amended)** A polyclonal or monoclonal antibody molecule that binds specifically to a FigE polypeptide or a derivative of a FigE polypeptide from *Lawsonia s*pp. wherein said derivative has at least about 60% sequence identity overall to the amino acid sequence set forth in SEQ ID NO: 1.

27. **(Amended)** A method of diagnosing the infection of a porcine or avian animal by *Lawsonia intracellularis* or a microorganism that is immunologically cross-reactive thereto, said method comprising the steps of: contacting a biological sample derived from said animal with the antibody molecule of claim 25 for a time and under conditions sufficient for an antigen:antibody complex to form, and detecting said complex formation.

28. **(Amended)** The method of claim 27 wherein the biological sample is selected from the group consisting of serum, lymph nodes, ileum, caecum, small intestine, large intestine, faeces or a rectal swab derived from a porcine animal.

29. **(Amended)** A method of identifying a previous or current infection with *Lawsonia intracellularis* or a microorganism that is immunologically cross-reactive thereto, said method comprising:

contacting blood or serum from said animal with the immunogenic polypeptide of claim 1 for a time and under conditions sufficient for an antigen: antibody complex to form; and detecting said complex formation.

30. **(Amended)** An isolated polynucleotide encoding a peptide, oligopeptide or polypeptide selected from the group consisting of:

(i) a peptide, oligopeptide or polypeptide which comprises an amino acid sequence which has at least about 60% sequence identity to the amino acid sequence set forth in SEQ ID NO: 1; and

(iii) a homologue or derivative of (i) which mimics a B-cell or T-cell epitope of or confers immunity against a Lawsonia spp *when injected into an animal.*

31. **(Amended)** The isolated polynucleotide of claim 30, wherein the peptide, oligopeptide or polypeptide comprises the amino acid sequence set forth in SEQ ID NO: 1 or the amino acid sequence encoded by the FigE-encoding nucleotide sequence of pALK11 (ATCC 207156) or a B-cell epitope or T-cell epitope thereof.

32. **(Amended)** The isolated polynucleotide of claim 31 comprising SEQ ID NO: 2, a complement or variant thereof.

33. **(Amended)** The isolated nucleic acid molecule of claim 32 consisting essentially of the nucleotide sequence of SEQ ID NO: 2 or a variant thereof.

34. **(Amended)** A method of detecting *Lawsonia intracellularis* or *Lawsonia spp* in a biological sample from a porcine or avian animal subject, said method comprising:

hybridizing one or more probes or primers from SEQ ID NO: 2 or a complement thereto to said sample; and detecting said hybridization .

35. **(Amended)** The method of claim 34 wherein the biological sample is selected from the group consisting of: serum, lymph nodes, ileum, caecum, small intestine, large intestine, faeces and a rectal swab from a porcine animal.

36. **(Amended)** The method of claim 34 wherein the detection is by any nucleic acid based hybridization or amplification reaction.

37. **(Amended)** A probe or primer comprising least about 15 contiguous nucleotides from SEQ ID NO: 2 or the complement thereof.

38. **(Amended)** The plasmid pALK13 (ATCC Accession No. 207196).

39. **(Amended)** The combination vaccine according to claim 21 wherein the second immunogenic component is selected from the group consisting of SodC, FIgE, hemolysin and autolysin.

REMARKS

The claims have been amended to more clearly recite the claimed invention under United States patent practice. Claims 5, 9, 12, 15, and 16 have been deleted. As a result of the amendment, Claims 1-4, 6-8, 10-11, 13-14, 17-39 are presented for examination.

The changes made to the claims by the current amdnemnt, including **[deletions]** and additions, are shown on an attached sheet entitiled **VERSION WITH MARKINGS TO SHOW CHANGES MADE**, which follows the signature page of this Amendment.

Int'l. Appl. No. : PCT/AU00/00437
Date : May 11, 2000

Please charge any additional fees, including any fees for additional extension of time, or credit overpayment to Deposit Account No. 11-1410.

Respectfully submitted,

KNOBBE, MARTENS, OLSON & BEAR, LLP

Dated: 13 Nov. 2001

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VERSION WITH MARKINGS TO SHOW CHANGES MADE

IN THE SPECIFICATION

On page 1, after the Title of the Invention (on line 1) and before the "Field of the Invention" (on line 4) please insert the following: --This is the U.S. National phase under 35 U.S.C. §371 of International application PCT/AU00/00437, filed May 11, 2000, and claim priority to U.S.Provisional Application 60/133973, filed May 13, 1999, both of which are herein incorporated by reference.--.

IN THE CLAIMS

Claims 5, 9, 12, 15, and 16 have been cancelled.

1. **(Amended)** An isolated or recombinant immunogenic polypeptide **[which comprises, mimics or cross-reacts with a B-cell or T-cell epitope of]**comprising a *Lawsonia spp.* FigE Polypeptide, a variant, or a truncated variant thereof, wherein said variant or truncated variant mimics or cross-reacts with a B-cell or T-cell epitope of *Lawsonia spp.* FigE Polypeptide.

2. **(Amended)** The isolated or recombinant immunogenic polypeptide of claim 1 **[capable of eliciting]**wherein said polypeptide elicits the production of antibodies against *Lawsonia* spp. when administered to an avian or porcine animal.

3. **(Amended)** The isolated or recombinant immunogenic polypeptide of claim 1 **[capable of conferring]**which confers a protective immune response against *Lawsonia spp.* when administered to an avian or porcine animal.

4. **(Amended)** The isolated or recombinant immunogenic polypeptide of claim **[2]**1 wherein the *Lawsonia spp. is L. intracellularis.*

6. **(Amended)** An isolated or recombinant immunogenic polypeptide **[selected from the following]**comprising:

    (i) *a peptide, oligopeptide or polypeptide **[which comprises]**comprising an amino acid sequence which has at least about 60% sequence identity **[overall]** to the amino acid sequence set forth in SEQ ID NO: 1;* or

    (ii) *a homologue**[, analogue]** or derivative of (i) which mimics a B-cell or T-cell epitope of a* Lawsonia spp. *FigE polypeptide.*

7. **(Amended)** The isolated or recombinant immunogenic polypeptide of claim 6 wherein said polypeptide **[capable of eliciting]**elicits the production of antibodies against *Lawsonia* spp. in a porcine or avian animal.

8. **(Amended)** The isolated or recombinant immunogenic polypeptide of claim **[7]**6 wherein said polypeptide **[capable of conferring]**confers a protective immune response against *Lawsonia spp. in* a porcine or avian animal.

10. **(Amended)** The isolated or recombinant immunogenic polypeptide of claim **[9]**8, **[capable of inducing humoral immunity against *Lawsonia* spp.]**wherein said protective immune response is induced in a porcine animal.

11. **(Amended)** The isolated or recombinant immunogenic polypeptide of claim **[8]**6 wherein the *Lawsonia spp.* is *L. intracellularis.*

13. **(Amended)** The isolated or recombinant immunogenic polypeptide of claim 6 **[that comprises]**comprising the amino acid sequence set forth in SEQ ID NO: 1 or the amino acid sequence encoded by the FigE-encoding nucleotide sequence of pALK11 (ATCC 207156)**[and is capable of eliciting the production of antibodies against *Lawsonia intracellularis* when administered to an avian or porcine animal]**.

14. **(Amended)** The isolated or recombinant immunogenic polypeptide of claim 13 **[that consists]**consisting essentially of the amino acid sequence of SEQ ID NO: 1 or the amino acid sequence encoded by the FigE-encoding nucleotide sequence of pALK11 (ATCC 207156).

17. **(Amended)** A vaccine composition for the prophylaxis or treatment of infection of an animal by *Lawsonia* spp., said vaccine composition comprising an immunogenic component **[which comprises]**comprising an isolated or recombinant polypeptide having at least about 60% sequence identity **[overall]** to the amino acid sequence set forth in SEQ ID NO: 1 or an immunogenic homologue, **[analogue]** or derivative thereof which is immunologically cross-reactive with *Lawsonia intracellularis;* and one or more carriers, diluents or adjuvants suitable for veterinary or pharmaceutical use.

19. **(Amended)** The vaccine composition according to claim **[18]**16 wherein the **[immunogenic component comprises an]** isolated or recombinant polypeptide **[that]** comprises the amino acid sequence set forth in SEQ ID NO: 1 or the amino acid sequence encoded by the FigE-encoding nucleotide sequence of pALK11 (ATCC 207156).

20. **(Amended)** The vaccine composition of claim 19, wherein the **[immunogenic component]**isolated or recombinant polypeptide consists essentially of the amino acid sequence of SEQ ID NO: 1.

21. **(Amended)** A combination vaccine composition for the prophylaxis or treatment of the infection of an animal by *Lawsonia* spp., said vaccine composition comprising:

(i) a first immunogenic component ***[which comprises]****comprising an isolated or recombinant polypeptide having at least about 60% sequence identity* ***[overall]*** *to the amino acid sequence set forth in SEQ ID NO: 1 or an immunogenic homologue****[, analogue]****or derivative thereof which is immunologically cross-reactive with* Lawsonia intracellularis;

(ii) a second immunogenic component comprising an antigenic L. intracellularis *peptide, polypeptide or protein; and*

(iii) one or more carriers, diluents or adjuvants suitable for veterinary or pharmaceutical use.

22. **(Amended)** A vaccine vector **[that comprises in an expressible form, an isolated nucleic acid molecule having a nucleotide sequence]**comprising a polynucleotide that encodes the **[an isolated or recombinant]** immunogenic polypeptide **[which comprises the amino acid sequence set forth in]**of SEQ ID NO: 1, a homologue or a variant thereof**[, such that said immunogenic polypeptide is expressible at a level sufficient to confer immunity against *Lawsonia* spp., when administered to a porcine or avian animal]**operably linked to a promoter.

23. **(Amended)** The vaccine vector of claim 22 wherein the **[immunogenic polypeptide is expressed using the steps of:**

(i) placing an isolated nucleic acid molecule which comprises the nucleotide sequence set forth in]polynucleotide comprises SEQ ID N0: 2 [or degenerate variant,] a homologue, [analogue] or derivative thereof which has at least about 60% sequence identity thereto[, in operable association with a promoter sequence;

(ii) introducing the isolated nucleic acid molecule and promoter sequence of step (a) into the vaccine vector; and

(iii) incubating, growing, or propagating the vaccine vector for a time and under conditions sufficient for expression of the immunogenic polypeptide encoded by said nucleic acid molecule to occur].

25. **(Amended)** A polyclonal or monoclonal antibody molecule that **[is capable of binding]**binds specifically to **[an]**a FigE polypeptide or a derivative of **[an]**a FigE polypeptide **[that is derived]** from *Lawsonia s*pp. **[and]**wherein said derivative has at least about 60% sequence identity **[overall]** to the amino acid sequence set forth in SEQ ID NO: 1.

27. **(Amended)** A method of diagnosing the infection of a porcine or avian animal by *Lawsonia intracellularis* or a microorganism that is immunologically cross-reactive thereto, said method comprising the steps of: contacting a biological sample derived from said animal with the antibody molecule of claim 25 for a time and under conditions sufficient for an antigen:antibody complex to form, and **[then]** detecting said complex formation.

28. **(Amended)** The method of claim 27 wherein the biological sample **[comprises whole]**is selected from the group consisting of serum, lymph nodes, ileum, caecum, small intestine, large intestine, faeces or a rectal swab derived from a porcine animal.

29. **(Amended)** A method of identifying **[whether or not a porcine or avian animal has suffered from a past infection, or is currently infected,]**a previous or current infection with *Lawsonia intracellularis* or a microorganism that is immunologically cross-reactive thereto, said method comprising:

contacting blood or serum **[derived]** from said animal with the immunogenic polypeptide of claim 1 for a time and under conditions sufficient for an antigen: antibody complex to form; and **[then]** detecting said complex formation.

30. **(Amended)** An isolated **[nucleic acid molecule which comprises a sequence of nucleotides which encodes, or is complementary to a nucleic acid molecule that encodes,]**polynucleotide encoding a peptide, oligopeptide or polypeptide selected from the group **[aconsisting]**consisting of:

*(i) a peptide, oligopeptide or polypeptide which comprises an amino acid sequence which has at least about 60% sequence identity **[overall]** to the amino acid sequence set forth in SEQ ID NO: 1; and*

*(iii) a homologue**[, analogue]** or derivative of (i) which mimics a B-cell or T-cell epitope of or confers immunity against a* Lawsonia spp *when injected into an animal.*

31. **(Amended)** The isolated **[nucleic acid molecule]**polynucleotide of claim 30, wherein the peptide, oligopeptide or polypeptide comprises the amino acid sequence set forth in SEQ ID NO: 1 or the amino acid sequence encoded by the FigE-encoding nucleotide sequence of pALK11 (ATCC 207156) or a B-cell epitope or T-cell epitope thereof.

32. **(Amended)** The isolated **[nucleic acid molecule]**polynucleotide of claim 31 comprising **[the nucleotide sequence set forth in]** SEQ ID NO: 2, **[or]** a **[complementary nucleotide sequence thereto, or a degenerate]**complement or variant thereof.

33. **(Amended)** The isolated nucleic acid molecule of claim 32 consisting essentially of the nucleotide sequence of SEQ ID NO: 2 or a **[degenerate]** variant thereof.

34. **(Amended)** A method of detecting *Lawsonia intracellularis* or **[related microorganism]***Lawsonia spp* in a biological sample **[derived]** from a porcine or avian animal subject, said method comprising: **[the steps of]**

[hybridising]hybridizing one or more probes or primers **[derived from the nucleotide sequence set forth in]** from SEQ ID NO: 2 or a **[complementary nucleotide sequence]**complement thereto to said sample; and **[then]** detecting said hybridization **[hybridisation using a detection means]**.

35. **(Amended)** The method of claim 34 wherein the biological sample **[comprises whole]**is selected from the group consisting of: serum, lymph nodes, ileum, caecum, small intestine, large intestine, faeces **[or]**and a rectal swab **[derived]** from a porcine animal.

36. **(Amended)** The method of claim 34 wherein the detection **[means comprises]**is by any nucleic acid based **[hybridisation]**hybridization or amplification reaction.

37. **(Amended)** A probe or primer **[having at]**comprising least about 15 contiguous nucleotides **[in length derived]** from SEQ ID NO: 2 or **[a complementary nucleotide sequence thereto]** the complement thereof.

38. **(Amended)** **[A]**The plasmid **[designated]** pALK11 (ATCC Accession No. 207156).

39. **(Amended)** The combination vaccine according to claim 21 wherein the second immunogenic component **[comprises an antigenic *L. intracellularis* peptide, polypeptide or protein selected from the group consisting of]**is selected from the group consisting of OmpH, SodC, hemolysin and autolysin.